Efficacy of Adding Venetoclax to Chemoimmunotherapy in Patients with Relapsed/Refractory T-Cell Prolymphocytic Leukemia

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INTRODUCTION

- T-PLL is a rare and aggressive disease with high rates of relapse.
- Long-term survival for patients with R/R T-PLL is rare, and the response to salvage therapies is short-lived.
- Venetoclax, a BCL2 inhibitor, has shown preclinical activity in T-PLL, and case series have reported high response rates in R/R P-PLL when combined with chemotherapy.

OBJECTIVES

- To evaluate response rates and outcomes in patients with R/R T-PLL treated with venetoclax as part of salvage therapy.

METHODS

- Retrospective analysis of patients diagnosed with R/R T-PLL who received venetoclax-based therapy between January 2018 and May 2024.

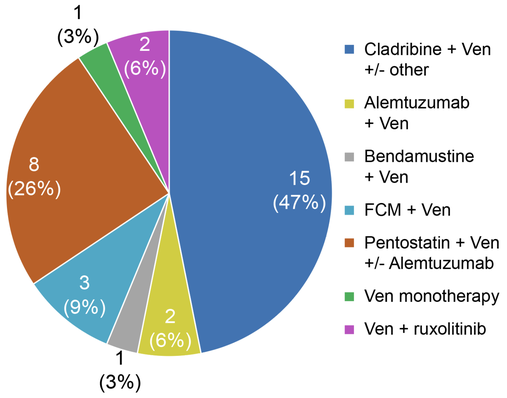
RESULTS

Table 1: Patient baseline characteristics*

Characteristic n (%) / median [range]	Patients (n=32)
Age (years)	65 [42-84]
Male	22 (69)
WBC (x10^9/L)	14 (0-514)
ALC (x10^9/L)	9 (0-483)
Hgb (g/dL)	10.5 (8.2-15.1)
Platelet count (x10^9/L)	66 (12-221)
LDH level (U/L)	491 (162-3,288)
Bone marrow involvement (%) (n=27)	68 (0-100)
Splenomegaly	17 (53)
Lymph node involvement	20 (63)
Extranodal involvement	13 (41)
Cytogenetic (n=30)	
Complex karyotype	18 (60)
inv(14) or t(14;14)	18 (60)
chromosome 8 abnormalities	15 (50)
TCL1 positive by FISH (n=28)	22 (79)
JAK3 mutation (n=22)	11 (50)
JAK1 mutation (n=22)	4 (18)
ATM mutation (n=22)	3 (14)
TP53 mutation (n=22)	1 (5)
Number of prior lines of therapy	1 [1-5]
Prior alemtuzumab	32 (100)
Prior HSCT	22 (69)

*Baseline characteristics were collected at the time of venetoclax initiation

Figure 1: Venetoclax-based therapy



- Median venetoclax dose: 600 (100-800)

RESULTS

Table 2: Clinical Outcomes

Clinical Outcomes	Patients (n=32)
Best response, n (%)	
CR*	5 (16)
CRi*	3 (9)
PR	8 (25)
NR	11 (34)
Not evaluable	5 (16)
ORR, n (%)	16 (50)
DOR, months (95% CI)	1.9 (0.9-3.0)

*Two patients with CR and one with CRi did not have bone marrow assessment at response, but met all other CR/CRi criteria

- 3/8 patients (38%) with CR/CRi achieved MRD negativity by flow cytometry
- Patients not evaluable for response had early mortality related to disease progression

Figure 2: OS of the entire cohort

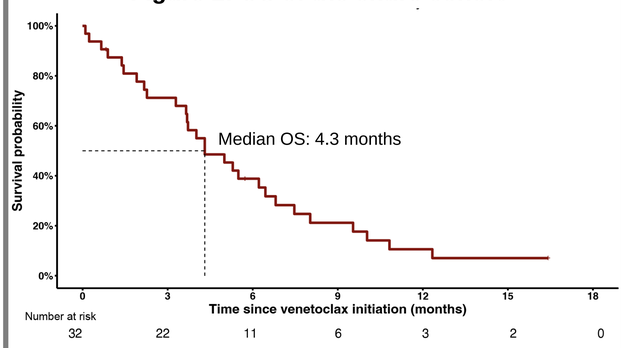
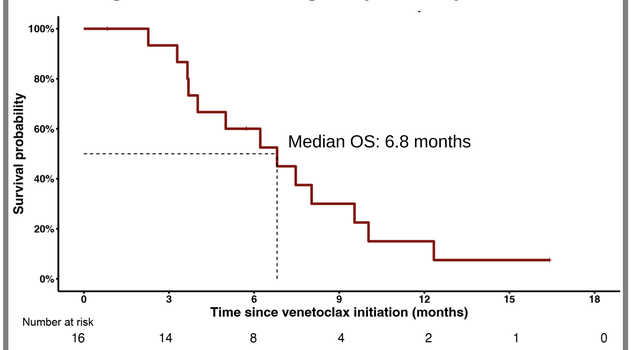


Figure 3: OS among responder patients



- Neutropenia grade ≥ 3: 24/30 (80%)
- Thrombocytopenia grade ≥ 3: 25/30 (83%)
- Tumor lysis syndrome: 3/32 (9%)
- Infection grade ≥ 3: 16/30 (53%)

CONCLUSION

- Patients with R/R T-PLL continue to face poor prognosis.
- Venetoclax-based therapies demostrated encouraging response rates. However, duration of response remains short.
- Prospective trials are need to optimize venetoclax-based treatment and post remission strategies for patients with R/R T-PLL.

CONTACT INFORMATION

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